

Attorney Docket No. GC560-D1-C1
Page 7

REMARKS

The original parent application (U.S. Patent Appln. Ser. No. 09/314,847, filed May 19, 1999, now U.S. Patent No. 6,365,410) was originally filed with 48 Claims. Patent No. 6,365,410 contains Claims that correspond to Claims 1-3, 11-24, and 28-48 of the originally filed application. In the currently pending Divisional application (U.S. Patent Appln. Ser. No. 10/037,677) to which the present Continuation application claims priority was filed on October 23, 2001, all of the Claims were cancelled and new Claims 49-58 (which correspond to originally filed Claims 4-10 and 25-27) were added. In a Preliminary Amendment filed November 20 2003, with the present Continuation application, original Claims 1-48 were cancelled and new Claims 49-71 added.

Applicants note that the Examiner has entered the Information Disclosure Statement and PTO-1449. Applicants also note that the Examiner has identified two informalities in the Specification. In the amendments provided in the present Response, these informalities have been corrected. No new matter is introduced by these amendments.

The Examiner's rejections are addressed in the following order:

- 1) Claims 49 and 61 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 3 of U.S. Patent No. 6,365,410;
- 2) Claims 49, 52-54, 56-57, 59 and 61-64 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-10 of U.S. Patent No. 6,705,503;
- 3) Claims 49-71 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to meet the written description requirement;
- 4) Claim 53 stands rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to meet the written description requirement; and
- 5) Claims 49 and 53 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Attorney Docket No. GC560-D1-C1
Page 8

1-2) There is No Double Patenting

The Examiner has rejected Claims 49 and 61, under the judicially-created doctrine of obviousness-type double patenting, as being allegedly unpatentable over Claim 3 of U.S. Patent No. 6,365,410 ("410 Patent"). The Examiner has also rejected Claims 49, 52-54, 56-57, 59 and 61-64 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-10 of U.S. Patent No. 6,705,503

In order to further their business interests and the present application, yet without acquiescing to the Examiner's arguments, Applicants will submit a Terminal Disclaimer upon receiving notification that the Claims are allowed.

3-4) The Written Description Requirement is Met

The Examiner has rejected Claims 49-71, under 35 U.S.C. §112, first paragraph, as allegedly failing to meet the written description requirement. The Examiner has also rejected Claim 53, under 35 U.S.C. §112, first paragraph, as allegedly failing to meet the written description requirement.

In regard to Claims 49-71, the Examiner argues that there is no "literal support in the originally filed specification for the terms 'producing' 'expresses' or 'isolating the heterologous protein. Therefore, the limitation s [sic] that the heterologous protein is 'produced' and the, [sic] the step of expressing and isolating the protein is impermissible NEW MATTER." (Office Action, page 5, emphasis original). Applicants must respectfully disagree. Throughout the Specification as filed, there are references to the expression of heterologous proteins by the evolved microorganisms of the present invention. For example, the originally filed Claims clearly recite the use of heterologous proteins and specifically provides for various enzymes as being the heterologous proteins. In addition, the "Field of the Invention" clearly indicates that the present invention provides for "the industrial production of heterologous proteins, such as hormones, growth factors and enzymes, and the biocatalytic production of chemicals, vitamins, amino acids and dyes."

The present Specification further indicates that "[i]n one embodiment, the microorganism further comprises at least one introduced nucleic acid encoding a heterologous protein, said protein(s) including, but not limited to hormones, enzymes, growth factors. In another embodiment, the enzyme includes, but is not limited to hydrolases, such as protease, esterase, lipase, phenol oxidase, permease, amylase, pullulanase, cellulase, glucose isomerase, laccase and protein disulfide isomerase. The present invention encompasses

Attorney Docket No. GC560-D1-C1
Page 9

genetic changes in the microorganism as well as changes in the introduced nucleic acid." (Specification, at page 3, lines 17-24).

The Specification further indicates that "[i]n yet a further embodiment, the microorganism further comprises introduced nucleic acid encoding at least one enzyme necessary for an enzymatic pathway. In one embodiment, the introduced nucleic acid is heterologous to the microorganism; in another, the introduced nucleic acid is homologous to the microorganism." (Specification, at page 3, lines 25-28).

The Specification further indicates that "[i]n another aspect of the present invention, the methods are used to evolve microorganisms which comprise introduced nucleic acid encoding a heterologous protein or at least one enzyme in an enzymatic, ie biocatalytic pathway. Such commercially important proteins include hormones, growth factors and enzymes."

(Specification, at page 9, lines 26-29).

The Specification also indicates that "[m]ethods of the present invention are especially advantageous for producing improved microorganisms used for the biocatalytic production of chemicals and vitamins where numerous catalytic events are taking place either concurrently or sequentially within the host microorganism. In such complex biocatalytic systems, it is often difficult to identify the specific molecular events causing low yields, host toxicity or catalytic failures and therefore difficult if not impossible to understand which specific genetic events to alter in order to correct the deficiencies. The methods of the present invention provide the advantage of allowing the microorganism to make the required changes in response to selective pressure." (Specification, at page 9, line 33, through page 10, line 6).

Applicants respectfully submit that although the Examiner may not be able to find the exact terms used as recited in the Claims, that it is clear in the Specification that the evolved microorganisms are used for the production of heterologous proteins. Furthermore, it would not meet the goal of the present invention to provide "commercially important proteins" (See, above) using the microorganisms of the present invention if the expressed heterologous proteins are not produced nor isolated. Thus, Applicants respectfully submit that the recitations in the Claims are not new matter, as support for the use of the claimed invention to produce heterologous proteins is clearly provided in the Specification as filed.

With regard to Claim 53, Applicants respectfully submit that this Claim does not recite any mutator genes. Based on the Examiner's arguments, Applicants believe that the Examiner actually meant Claim 55. Thus, this Response applies to Claim 55, rather than Claim 53. Although Applicants respectfully submit that the Claim is definite as filed, in order to further the

Attorney Docket No. GC560-D1-C1
Page 10

prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have cancelled Claim 55 and amended Claim 56 to specifically recite mutations of *mutD*. The Examiner admits that the Specification discloses nucleic acid and amino acid sequences for *mutD*. (Office Action, page 6). As there is more than sufficient support in the Specification for this amendment, Applicants submit that no new matter is added by this amendment. As there is clear support for this amendment, Applicants respectfully submit that the written description requirement is met. Indeed, as the Specification clearly describes the use of *mutD*, Applicants respectfully request that this rejection be withdrawn.

5) The Claims are Definite

The Examiner has rejected Claims 49 and 53 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. In particular, the Examiner argues the Claim 49 "does not set forth any steps for the production of a protein." (Office Action, page 7). In regard to Claim 53, the Examiner argues that "the metes and bounds of 'the mutator gene' are unclear. The mutator gene is selected from the group consisting of *mutD*, *mutT*, *mutY*, *mutM*, *mutH*, *mutL*, *mutS*, and *mutU* mutations. A mutator gene is a DNA repair gene with a mutation. However, the previous list of genes encode wild type DNA repair proteins and as recited, it is unclear how the genes can be mutator genes." (Office Action, page 7). The Examiner also argues that Claim 53 is vague and indefinite in that the metes and bounds of "*mutU* mutations" are unclear. It is unclear [sic] *mutU* mutations can be a mutator genes [sic]. Mutations [sic] *mutU* can generate a mutator gene but the mutations themselves cannot be mutator genes." (Office Action, page 8).

With regard to Claim 49, Applicants must respectfully submit that the Claim is definite as submitted. However, in order to more clearly recite the method, Applicants have amended the Claim to recite that the heterologous protein is expressed by the microorganism. Thus, Applicants respectfully submit that the Claim is definite and request that this rejection be withdrawn.

With regard to Claim 53, Applicants respectfully submit that this Claim does not recite any mutator genes. Based on the Examiner's arguments, Applicants believe that the Examiner actually meant Claim 55. Thus, this Response applies to Claim 55, rather than Claim 53. Although Applicants respectfully submit that the Claim is definite as filed, in order to further the prosecution of the present application and Applicants' business interests, yet without

Attorney Docket No. GC560-D1-C1
Page 11

acquiescing to the Examiner's arguments, Applicants have cancelled Claim 55 and amended Claim 56 to specifically recite mutations of *mutD*. As there is more than sufficient support in the Specification for this amendment, Applicants submit that no new matter is added by this amendment. As there is clear support for this amendment, Applicants respectfully submit that the amended Claims are definite. Indeed, as the Specification clearly describes the use of *mutD*, Applicants respectfully request that this rejection be withdrawn.

Attorney Docket No. GC560-D1-C1
Page 12

CONCLUSION

In light of the above remarks, the Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application and/or if there are any questions regarding the present Response and/or application, the Examiner is invited to telephone the undersigned at (650) 846-5838.

Respectfully submitted,

Date: December 17, 2004



Kamrin T. MacKnight
Registration No. 38,230

Genencor International, Inc.
925 Page Mill Road
Palo Alto, CA 94304
Tel: 650-846-5838
Fax: 650-845-6504